

4/29/05

ANSWER 1 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2005:23545 CAPLUS
 DOCUMENT NUMBER: 142:261320
 TITLE: Ring-Closing Metathesis Approach to Dictyostatin
 AUTHOR(S): Kangani, Cyrus O.; Brueckner, Arndt M.; Curran, Dennis P.
 CORPORATE SOURCE: Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA
 SOURCE: Organic Letters (2005), 7(3), 379-382
 CODEN: ORLEF7; ISSN: 1523-7060
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI

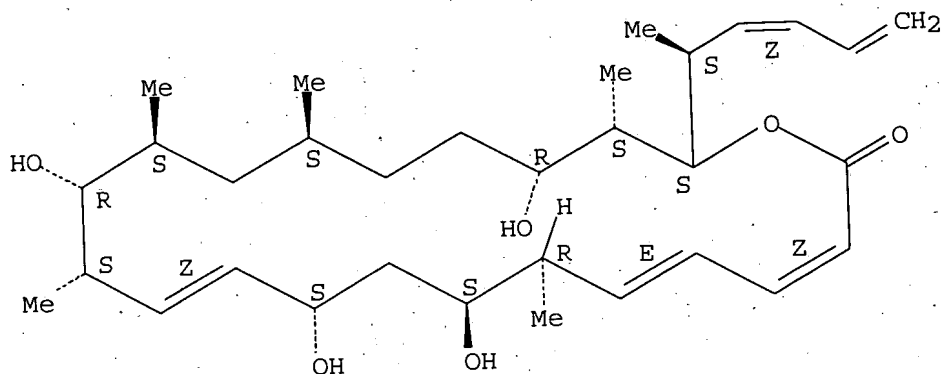
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB An esterification/ring-closing metathesis approach to dictyostatin and discodermolide intermediate I via II is introduced. The approach provides for facile fragment coupling of two main segments of these natural products at the C10-C11 alkene with high to complete Z-selectivity.

IT 156312-07-1P, Dictyostatin
 RL: PNU (Preparation, unclassified); PREP (Preparation) (ring-closing metathesis approach to dictyostatin)

RN 156312-07-1 CAPLUS
 CN Oxacyclodocosa-3,5,11-trien-2-one, 8,10,14,20-tetrahydroxy-7,13,15,17,21-pentamethyl-22-[(1S,2Z)-1-methyl-2,4-pentadienyl]-, (3Z,5E,7R,8S,10S,11Z,13S,14R,15S,17S,20R,21S,22S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
 Double bond geometry as described by E or Z.



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2004:782447 CAPLUS
 DOCUMENT NUMBER: 141:410752
 TITLE: Total synthesis of (-)-dictyostatin: Confirmation of relative and absolute configurations
 AUTHOR(S): Shin, Youseung; Fournier, Jean-Hugues; Fukui, Yoshikazu; Brueckner, Arndt M.; Curran, Dennis P.
 CORPORATE SOURCE: Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA
 Angewandte Chemie, International Edition (2004),

PUBLISHER:
DOCUMENT TYPE:
LANGUAGE:
GI

CODEN: ACIEF5; ISSN: 1433-7851
Wiley-VCH Verlag GmbH & Co. KGaA
Journal
English

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A total synthesis of (-)-dictyostatin (I) has ended the decade-old masquerade and identified the winner as a structure recently proposed by Paterson and Wright. Our synthesis utilized 3 key fragments, phosphonate ester II, disilylated alkyne III, and enal IV. III was metalated and added to IV to give an alkynyl ketone which was asym. reduced. The latter resulting compound was then subjected to Lindlar hydrogenation to give adduct V as a single isomer. Several further transformations, including a coupling reaction with II, gave I.

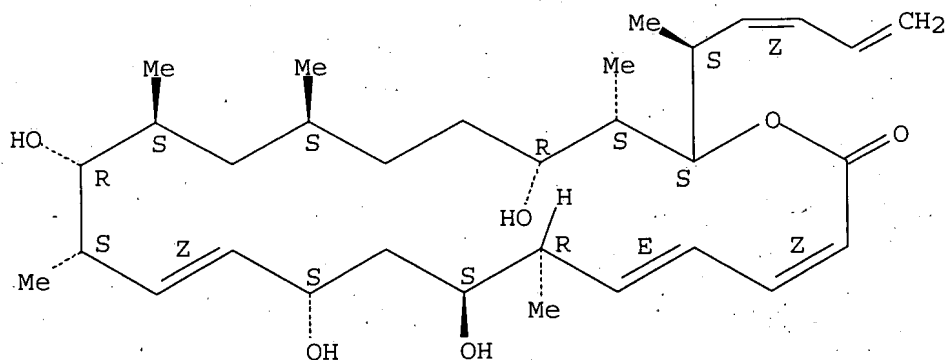
IT 156312-07-1P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of (-)-dictyostatin and confirmation of absolute configuration)

RN 156312-07-1 CAPLUS

CN Oxacyclodocosa-3,5,11-trien-2-one, 8,10,14,20-tetrahydroxy-7,13,15,17,21-pentamethyl-22-[(1S,2Z)-1-methyl-2,4-pentadienyl]-, (3Z,5E,7R,8S,10S,11Z,13S,14R,15S,17S,20R,21S,22S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



IT 792921-91-6P

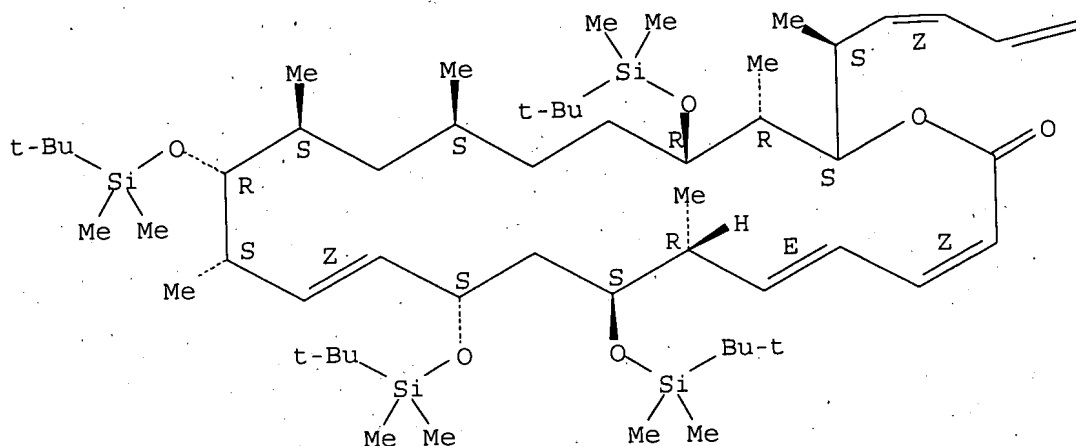
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(total synthesis of (-)-dictyostatin and confirmation of absolute configuration)

RN 792921-91-6 CAPLUS

CN Oxacyclodocosa-3,5,11-trien-2-one, 8,10,14,20-tetrakis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7,13,15,17,21-pentamethyl-22-[(1S,2Z)-1-methyl-2,4-pentadienyl]-, (3Z,5E,7R,8S,10S,11Z,13S,14R,15S,17S,20R,21R,22S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A

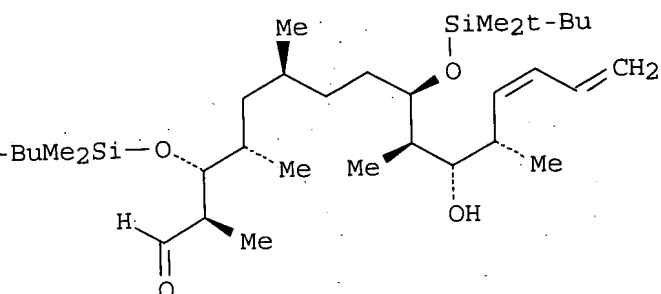
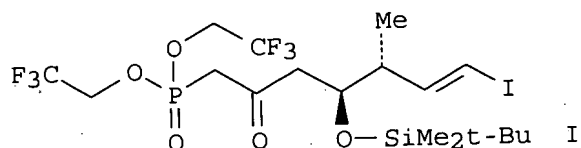


PAGE 1-B

=CH₂

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2004:782446 CAPLUS
 DOCUMENT NUMBER: 141:410751
 TITLE: Total synthesis and configurational assignment of (-)-dictyostatin, a microtubule-stabilizing macrolide of marine sponge origin
 AUTHOR(S): Paterson, Ian; Britton, Robert; Delgado, Oscar; Meyer, Arndt; Poullennec, Karine G.
 CORPORATE SOURCE: University Chemical Laboratory, Cambridge, CB2 1EW, UK
 SOURCE: Angewandte Chemie, International Edition (2004), 43(35), 4629-4633
 CODEN: ACIEF5; ISSN: 1433-7851
 PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



II

B A flexible and modular approach was used in the convergent and highly stereocontrolled synthesis of the antimitotic agent dictyostatin. A key step was the Gennari-type HWE coupling of phosphonate I with aldehyde II. This first total synthesis establishes its full stereochem. and should be amenable to producing useful quantities and designed analogs of this mol., whose conformation closely resembles that of discodermolide.

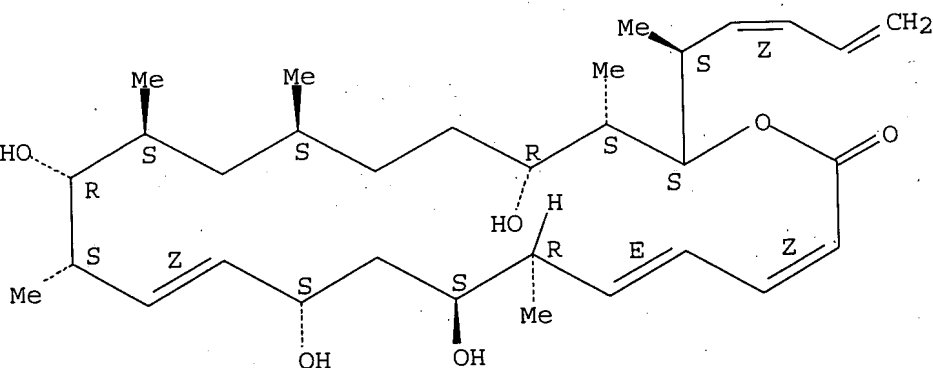
T **156312-07-1P**, (-)-Dictyostatin

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(absolute configuration of (-)-dictyostatin by its asym. total synthesis via Horner-Wadsworth-Emmons reaction, Stille cross-coupling, Yamaguchi macrolactonization, and reduction)

RN **156312-07-1** CAPLUS

CN Oxacyclodocosa-3,5,11-trien-2-one, 8,10,14,20-tetrahydroxy-7,13,15,17,21-pentamethyl-22-[(1S,2Z)-1-methyl-2,4-pentadienyl]-, (3Z,5E,7R,8S,10S,11Z,13S,14R,15S,17S,20R,21S,22S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry: Rotation (-).
Double bond geometry as described by E or Z.



IT **792911-15-0P 792911-33-2P**

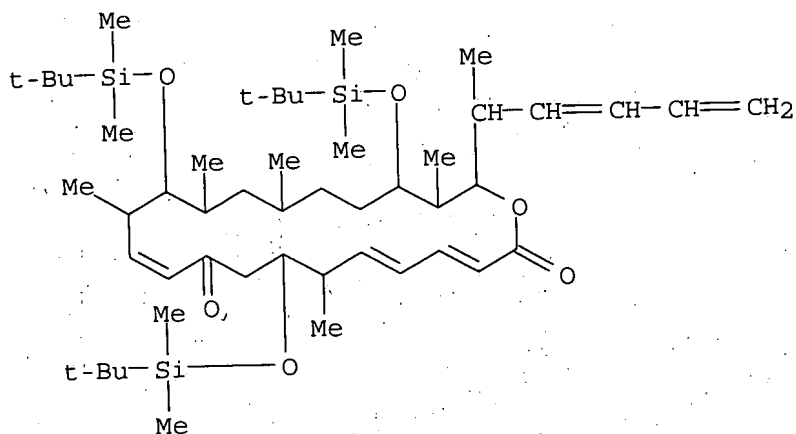
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(absolute configuration of (-)-dictyostatin by its asym. total synthesis via Horner-Wadsworth-Emmons reaction, Stille cross-coupling, Yamaguchi macrolactonization, and reduction)

RN **792911-15-0** CAPLUS

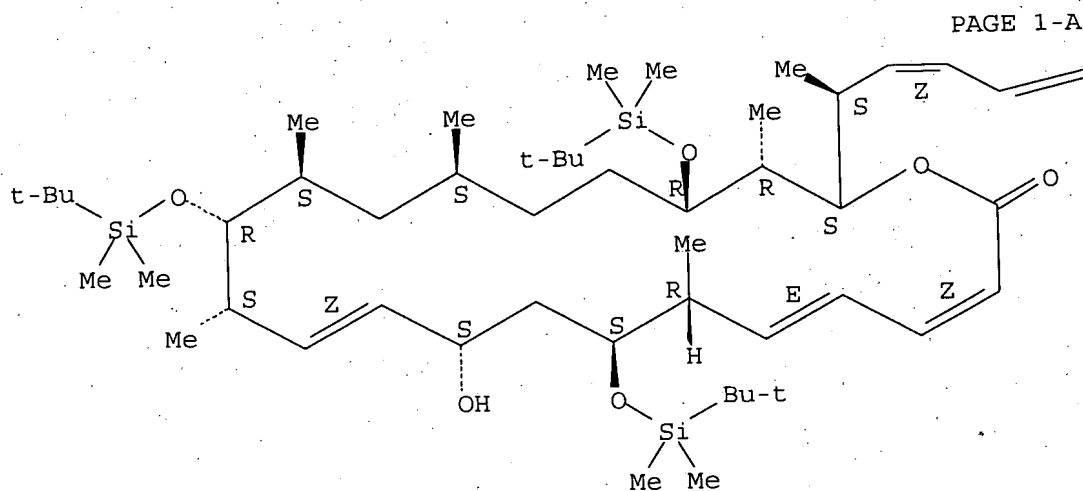
1,3,5,11-triene-2,10-dione 8,14,20-tris[[[(1,1-

methyl-2,4-pentadienyl]-, (3Z,5E,7S,8R,11Z,13R,14S,15R,17R,20S,21S,22R)-
rel- (9CI) (CA INDEX NAME)



RN 792911-33-2 CAPLUS
CN Oxacyclodocosa-3,5,11-trien-2-one, 8,14,20-tris[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-10-hydroxy-7,13,15,17,21-pentamethyl-22-[(1R,2Z)-1-methyl-2,4-pentadienyl]-, (3Z,5E,7S,8R,10R,11Z,13R,14S,15R,17R,20S,21S,22R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as described by E or Z.



PAGE 1-B

=CH₂

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:220327 CAPLUS
DOCUMENT NUMBER: 140:270672
Preparation of analogs of discodermolide and

INVENTOR(S): antiproliferative and microtubule stabilizing agents
Curran, Dennis P.; Shin, Youseung; Choy, Nakyne; Day,
Billy W.; Balachandran, Raghavan; Madiraju, Charitha;
Turner, Tiffany

PATENT ASSIGNEE(S): University of Pittsburgh, USA

SOURCE: PCT Int. Appl., 132 pp.
CODEN: PIXXD2

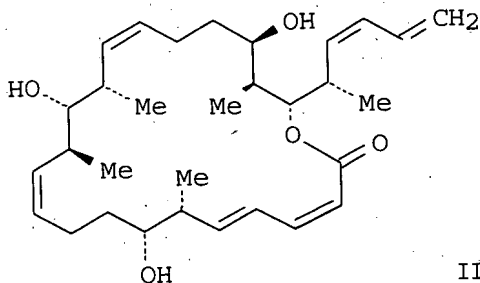
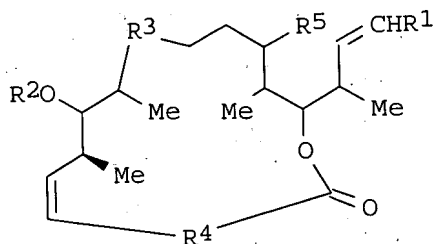
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004022552	A1	20040318	WO 2003-US327793	20030905
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004186165	A1	20040923	US 2003-655916	20030905
PRIORITY APPLN. INFO.:			US 2002-408503P	P 20020906
			US 2003-437736P	P 20030102
OTHER SOURCE(S):			CASREACT 140:270672; MARPAT 140:270672	
GI				



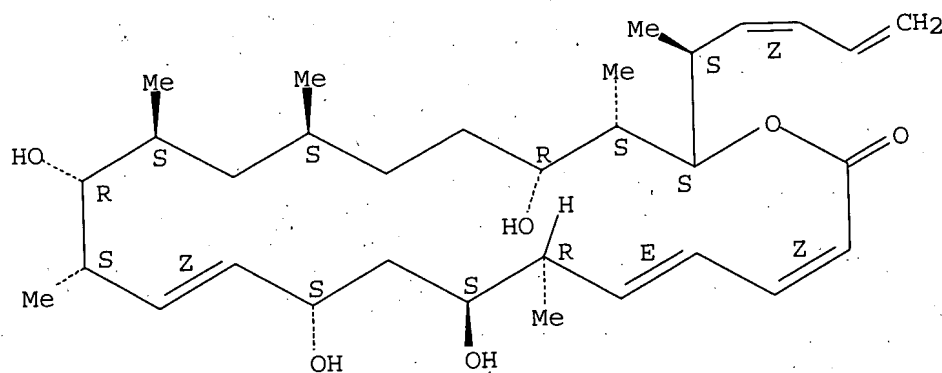
AB The present invention discloses preparation of analogs of discodermolide and dictyostatin-1, such as I [R1 = H, alkyl, aryl, alkenyl, alkynyl, halogen; R2 = H, alkyl, aryl, benzyl, trityl, SiR_aR_bR_c, CH₂OR_d, CORE; R_a, R_b, R_c = alkyl, aryl; R_d = alkyl, aryl, alkoxyalkyl, R_iSiR_aR_bR_c, benzyl; R_i = alkylene; R_e = alkyl, allyl, benzyl, aryl, alkoxy, NR_gR_h; R_g, R_h = H, alkyl, aryl; R₃ = (CH₂)_n; n = 0-5, CH₂CH(CH₃), CH:CH, CH:C(CH₃), C.tplbond.C; R₄ = (CH₂)_p; p = 4-12, etc.], are prepared for their therapeutic use as antiproliferative and microtubule stabilizing agents. Thus, dictyostatin-1 analog II was prepared via a multistep reaction sequence starting from Me (2S)-3-hydroxy-2-methylpropionate, (4R)-4-benzyl-3-propionyloxazolidin-2-one, p-anisaldehyde-dimethylacetal, 4-(tert-butyltrimethylsiloxy)butanal, 2,6-dimethylphenoxy propionate, 1-bromoallyl trimethylsilane and bis(2,2,2-trifluoroethyl)-(methoxycarbonylmethyl)phosphate. II exhibited antiproliferative activity, GI₅₀(μM) = 1.4±0.1 and 1.4±0.1 resp., against breast and ovarian cancer cells.

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of analogs of discodermolide and dictyostatin-1 and their use as antiproliferative and microtubule stabilizing agents)

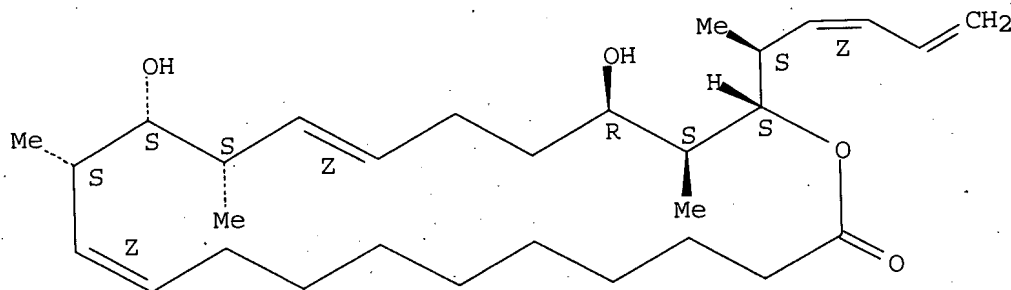
RN 156312-07-1 CAPLUS
CN Oxacyclodocosa-3,5,11-trien-2-one, 8,10,14,20-tetrahydroxy-7,13,15,17,21-pentamethyl-22-[(1S,2Z)-1-methyl-2,4-pentadienyl]-, (3Z,5E,7R,8S,10S,11Z,13S,14R,15S,17S,20R,21S,22S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



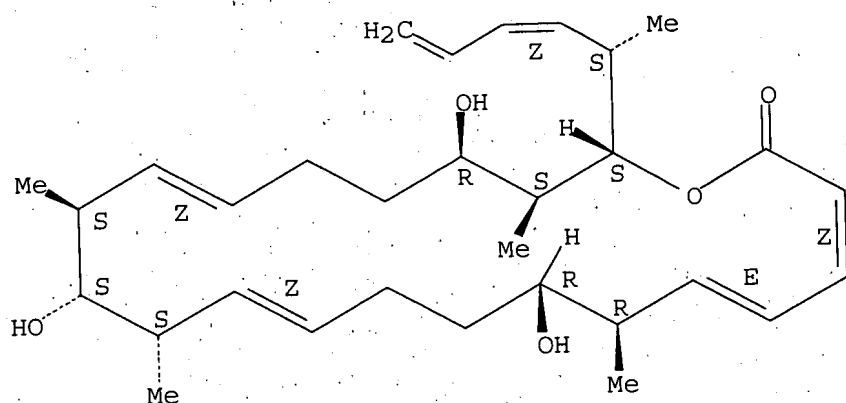
RN 479673-21-7 CAPLUS
CN Oxacyclodocosa-11,16-dien-2-one, 14,20-dihydroxy-13,15,21-trimethyl-22-[(1S,2Z)-1-methyl-2,4-pentadienyl]-, (11Z,13S,14S,15S,16Z,20R,21S,22S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as described by E or Z.



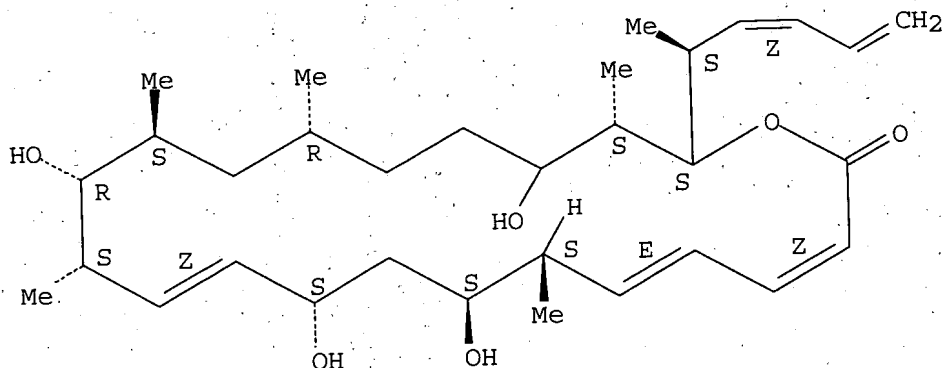
RN 479673-35-3 CAPLUS
CN Oxacyclodocosa-3,5,11,16-tetraen-2-one, 8,14,20-trihydroxy-7,13,15,21-tetramethyl-22-[(1S,2Z)-1-methyl-2,4-pentadienyl]-, (3Z,5E,7R,8R,11Z,13S,14S,15S,16Z,20R,21S,22S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as described by E or Z.



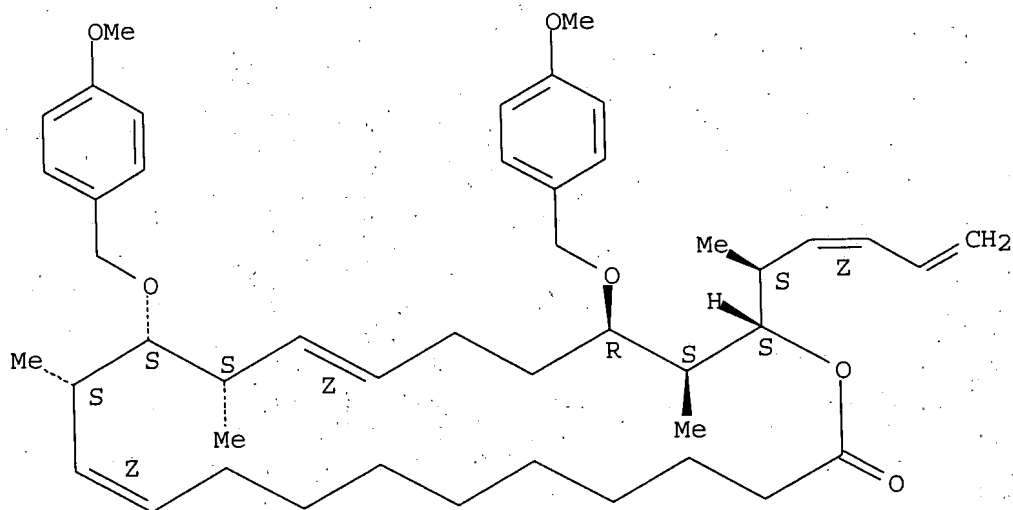
RN 674287-58-2 CAPLUS
 CN Oxacyclodocosa-3,5,11-trien-2-one, 8,10,14,20-tetrahydroxy-7,13,15,17,21-pentamethyl-22-[(1S,2Z)-1-methyl-2,4-pentadienyl]-, (3Z,5E,7S,8S,10S,11Z,13S,14R,15S,17R,21S,22S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as described by E or Z.



IT 479673-47-7P 479673-57-9P 672296-56-9P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of analogs of discodermolide and dictyostatin-1 and their use as antiproliferative and microtubule stabilizing agents)
 RN 479673-47-7 CAPLUS
 CN Oxacyclodocosa-11,16-dien-2-one, 14,20-bis[(4-methoxyphenyl)methoxy]-13,15,21-trimethyl-22-[(1S,2Z)-1-methyl-2,4-pentadienyl]-, (11Z,13S,14S,15S,16Z,20R,21S,22S) - (9CI) (CA INDEX NAME)

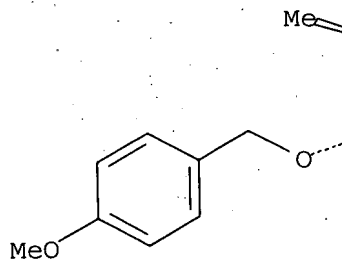
Absolute stereochemistry. Rotation (+).
 Double bond geometry as described by E or Z.



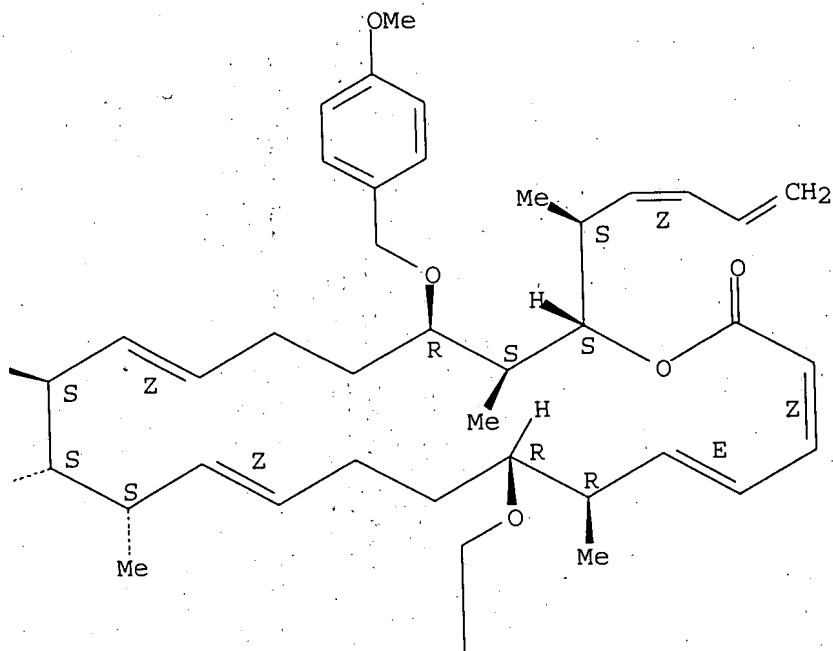
RN 479673-57-9 CAPLUS
 CN Oxacyclodocosa-3,5,11,16-tetraen-2-one, 8,14,20-tris[(4-methoxyphenyl)methoxy]-7,13,15,21-tetramethyl-22-[(1S,2Z)-1-methyl-2,4-pentadienyl]-, (3Z,5E,7R,8R,11Z,13S,14S,15S,16Z,20R,21S,22S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
 Double bond geometry as described by E or Z.

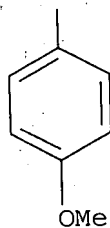
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PAGE 1-B

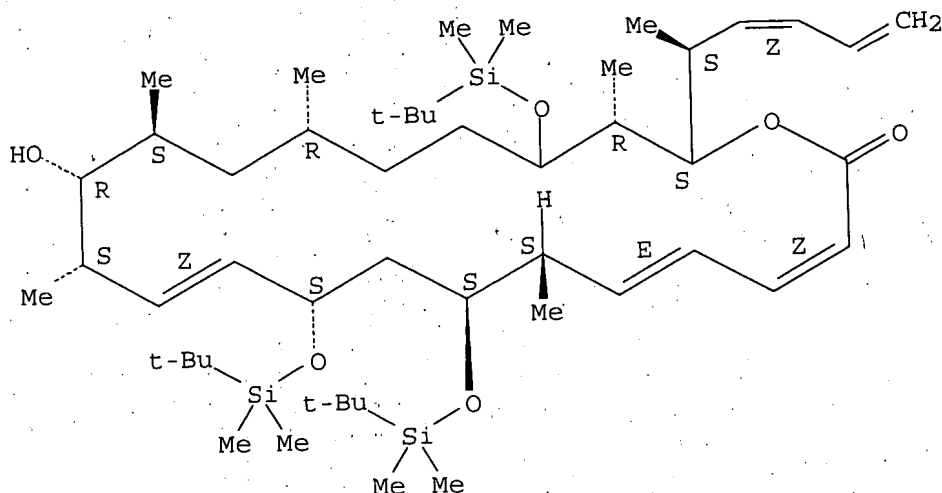


PAGE 2-B



RN 672296-56-9 CAPLUS
CN Oxacyclodocosa-3,5,11-trien-2-one, 8,10,20-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-14-hydroxy-7,13,15,17,21-pentamethyl-22-[(1S,2Z)-1-methyl-2,4-pentadienyl]-, (3Z,5E,7S,8S,10S,11Z,13S,14R,15S,17R,21R,22S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:197059 CAPLUS

DOCUMENT NUMBER: 141:6953

TITLE: Stereochemical determination of dictyostatin, a novel microtubule-stabilizing macrolide from the marine sponge Corallistidae sp.

AUTHOR(S): Paterson, Ian; Britton, Robert; Delgado, Oscar; Wright, Amy E.

CORPORATE SOURCE: University Chemical Laboratory, Cambridge, CB2 1EW, UK

SOURCE: Chemical Communications (Cambridge, United Kingdom)

(2004), (6), 632-633

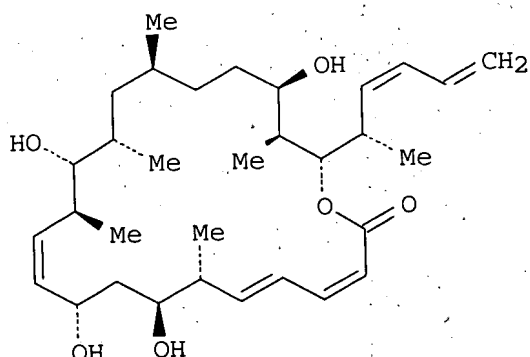
CODEN: CHCOFS; ISSN: 1359-7345

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



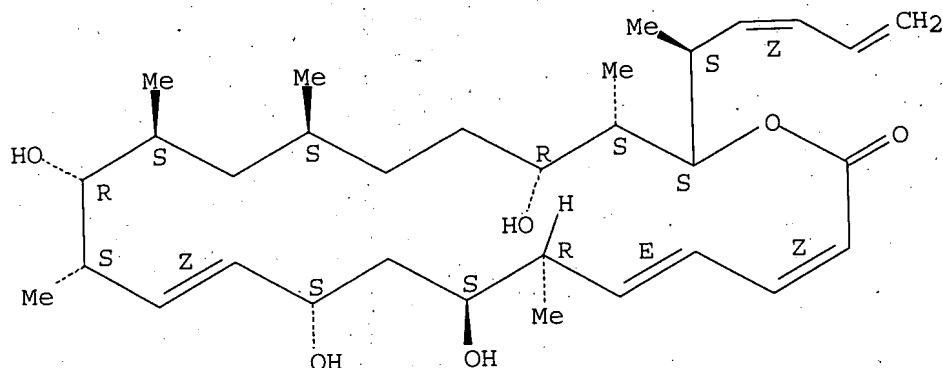
I

AB The relative stereochem. of the 22-membered marine macrolide dictyostatin (I), a Taxol-like antimitotic agent (no data), was determined based on a combination of extensive high field NMR studies, including J-based configuration anal., and mol. modeling.

(stereochem. determination of dictyostatin, a novel microtubule-stabilizing macrolide from the marine sponge Corallistidae sp.)

RN 156312-07-1 CAPLUS
CN Oxacyclodocosa-3,5,11-trien-2-one, 8,10,14,20-tetrahydroxy-7,13,15,17,21-pentamethyl-22-[(1S,2Z)-1-methyl-2,4-pentadienyl]-, (3Z,5E,7R,8S,10S,11Z,13S,14R,15S,17S,20R,21S,22S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry: Rotation (-).
Double bond geometry as described by E or Z.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

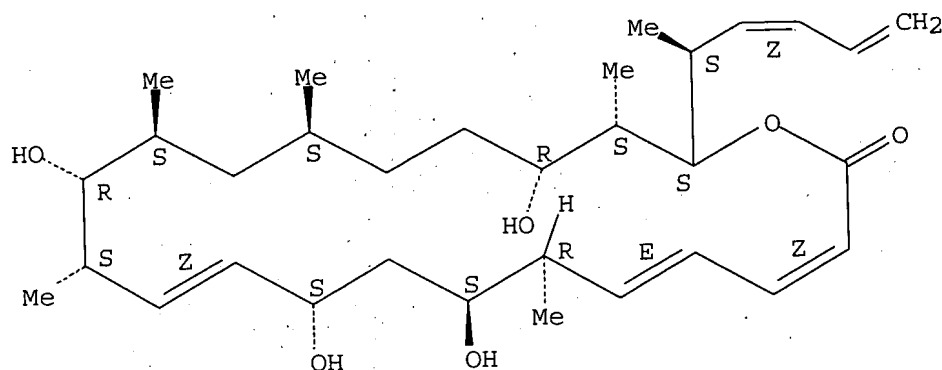
L3 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:461765 CAPLUS
DOCUMENT NUMBER: 139:358179
TITLE: Tubulin polymerizing activity of dictyostatin-1, a polyketide of marine sponge origin
AUTHOR(S): Isbrucker, Richard A.; Cummins, Jennifer; Pomponi, Shirley A.; Longley, Ross E.; Wright, Amy E.
CORPORATE SOURCE: Division of Biomedical Marine Research, Harbor Branch Oceanographic Institution, Inc., Fort Pierce, FL, 34946, USA
SOURCE: Biochemical Pharmacology (2003), 66(1), 75-82
CODEN: BCPA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Dictyostatin-1 had previously been isolated from a marine sponge of the genus Spongia sp. and described as a cytotoxic agent to murine and human cancer cells, but its mechanism of activity was unknown. In a routine screening assay used to detect cytotoxic compds. of marine origin, dictyostatin-1 was identified as a highly active component in an extract from a Lithistida sponge and exploration into its pharmacol. was pursued. Initial studies demonstrated that dictyostatin-1 arrested cells in the G2/M phase of the cell cycle. Staining of these cells with antitubulin revealed cells having multiple aster formations and microtubule matrix bundling patterns similar to that seen in cells exposed to paclitaxel. Dictyostatin-1 was able to induce the polymerization of purified bovine brain tubulin in vitro and the polymerized tubulin remained stable at cold temps. Dictyostatin-1 also proved to be highly potent in two paclitaxel-resistant human cancer cell lines expressing active P-glycoprotein. Together, these results indicate that dictyostatin-1 is a potent inducer of tubulin polymerization and retains activity in cells expressing the P-glycoprotein efflux pump.

IT 156312-07-1, Dictyostatin-1
(mechanism of action): PAC (Pharmacological activity); THU

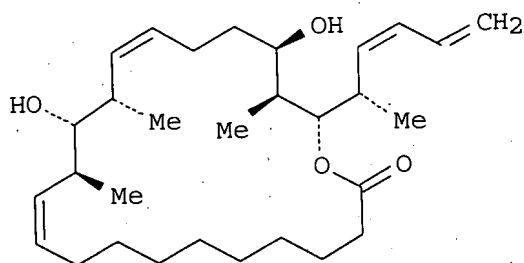
(tubulin polymerizing activity of dictyostatin-1)
 RN 156312-07-1 CAPLUS
 CN Oxacyclodocosa-3,5,11-trien-2-one, 8,10,14,20-tetrahydroxy-7,13,15,17,21-pentamethyl-22-[(1S,2Z)-1-methyl-2,4-pentadienyl]-, (3Z,5E,7R,8S,10S,11Z,13S,14R,15S,17S,20R,21S,22S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
 Double bond geometry as described by E or Z.

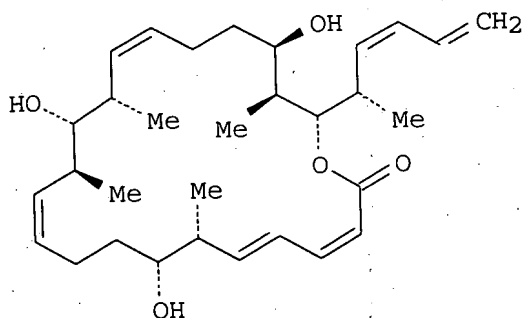


REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2002:870413 CAPLUS
 DOCUMENT NUMBER: 138:73122
 TITLE: Discodermolide/Dictyostatin Hybrids: Synthesis and Biological Evaluation
 AUTHOR(S): Shin, Youseung; Choy, Nakyeon; Balachandran, Raghavan; Madiraju, Charitha; Day, Billy W.; Curran, Dennis P.
 CORPORATE SOURCE: Department of Chemistry and Department of Pharmaceutical Sciences, University of Pittsburgh, Pittsburgh, PA, 15260, USA
 SOURCE: Organic Letters (2002), 4(25), 4443-4446
 CODEN: ORLEF7; ISSN: 1523-7060
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 138:73122
 GI



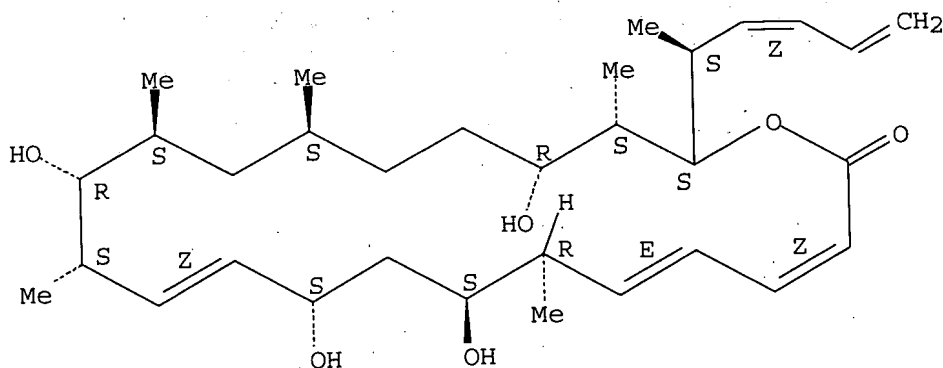
I



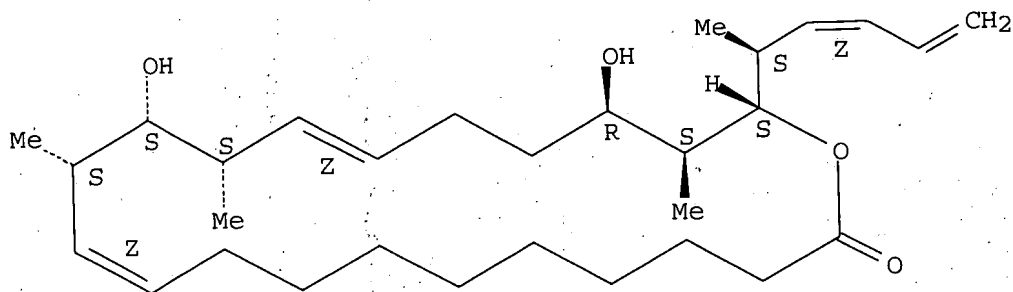
II

- AB Two hybrid analogs of discodermolide and dictyostatin (I, II) were designed and synthesized. These are the first macrocyclic analogs of discodermolide and biol. activities were evaluated and compared with linear discodermolide analogs.
- IT 156312-07-1DP, Dictyostatin-1, analogs 479673-21-7P
479673-35-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of discodermolide/dictyostatin hybrids from three asym. fragments and evaluation of their antitumor activity in human cancer cell lines)
- RN 156312-07-1 CAPLUS
- CN Oxacyclodocosa-3,5,11-trien-2-one, 8,10,14,20-tetrahydroxy-7,13,15,17,21-pentamethyl-22-[(1S,2Z)-1-methyl-2,4-pentadienyl]-, (3Z,5E,7R,8S,10S,11Z,13S,14R,15S,17S,20R,21S,22S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.

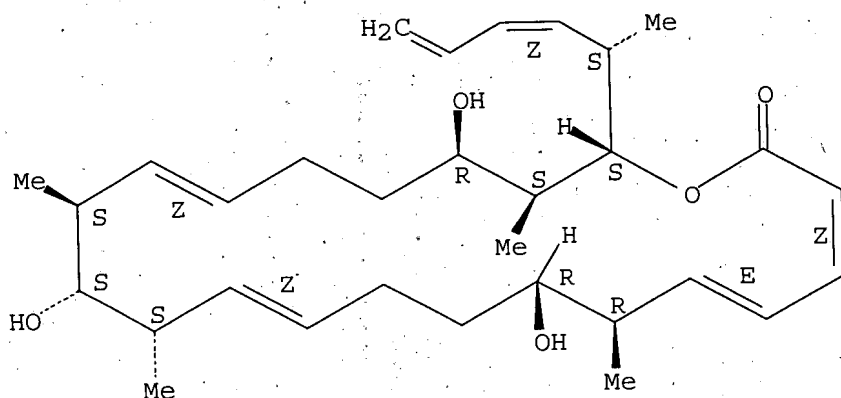


- RN 479673-21-7 CAPLUS
- CN Oxacyclodocosa-11,16-dien-2-one, 14,20-dihydroxy-13,15,21-trimethyl-22-[(1S,2Z)-1-methyl-2,4-pentadienyl]-, (11Z,13S,14S,15S,16Z,20R,21S,22S)- (9CI) (CA INDEX NAME)



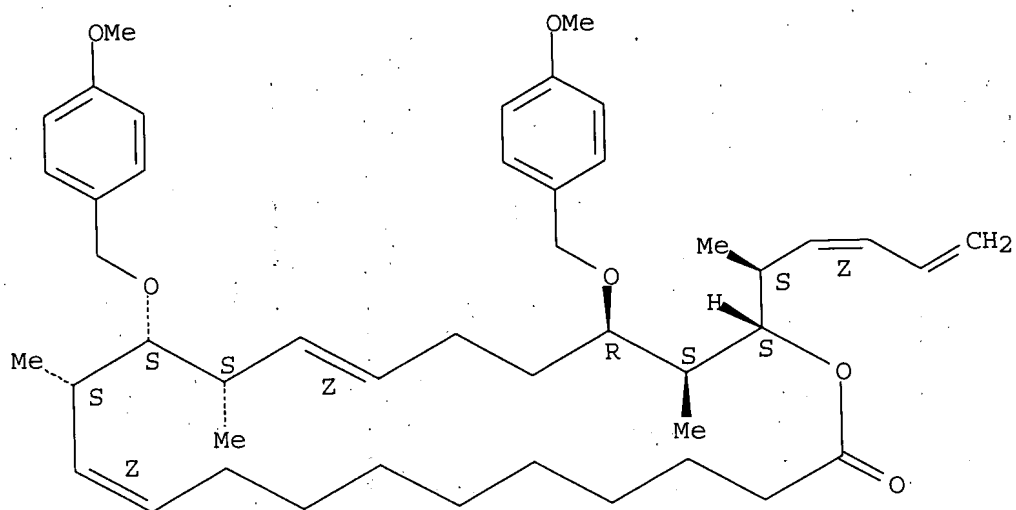
RN 479673-35-3 CAPLUS
 CN Oxacyclodocosa-3,5,11,16-tetraen-2-one, 8,14,20-trihydroxy-7,13,15,21-tetramethyl-22-[(1S,2Z)-1-methyl-2,4-pentadienyl]-, (3Z,5E,7R,8R,11Z,13S,14S,15S,16Z,20R,21S,22S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
 Double bond geometry as described by E or Z.



IT 479673-47-7P 479673-57-9P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of discodermolide/dictyostatin hybrids from three asym. fragments and evaluation of their antitumor activity in human cancer cell lines)
 RN 479673-47-7 CAPLUS
 CN Oxacyclodocosa-11,16-dien-2-one, 14,20-bis[(4-methoxyphenyl)methoxy]-13,15,21-trimethyl-22-[(1S,2Z)-1-methyl-2,4-pentadienyl]-, (11Z,13S,14S,15S,16Z,20R,21S,22S)- (9CI) (CA INDEX NAME)

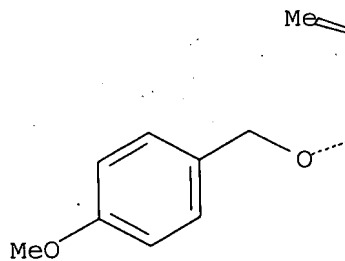
Absolute stereochemistry. Rotation (+).
 Double bond geometry as described by E or Z.



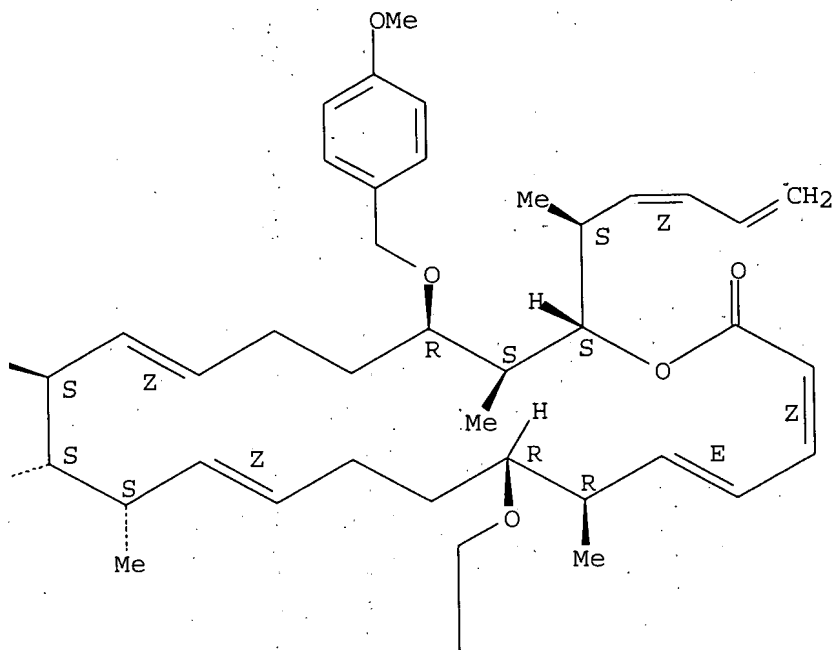
RN 479673-57-9 CAPLUS
 CN Oxacyclodocosa-3,5,11,16-tetraen-2-one, 8,14,20-tris[(4-methoxyphenyl)methoxy]-7,13,15,21-tetramethyl-22-[(1S,2Z)-1-methyl-2,4-pentadienyl]-, (3Z,5E,7R,8R,11Z,13S,14S,15S,16Z,20R,21S,22S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
 Double bond geometry as described by E or Z.

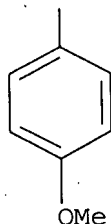
PAGE 1-A



PAGE 1-B



PAGE 2-B



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2001:635882 CAPLUS
 DOCUMENT NUMBER: 135:200474
 TITLE: Dictyostatin compounds for stabilization of microtubules
 INVENTOR(S): Wright, Amy E.; Cummins, Jennifer L.; Pomponi, Shirley A.; Longley, Ross E.; Isbrucker, Richard A.
 PATENT ASSIGNEE(S): Harbor Branch Oceanographic Institution, Inc., USA
 SOURCE: PCT Int. Appl., 30 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062239	A2	20010830	WO 2001-US6198	20010226
WO 2001062239	A3	20020124		

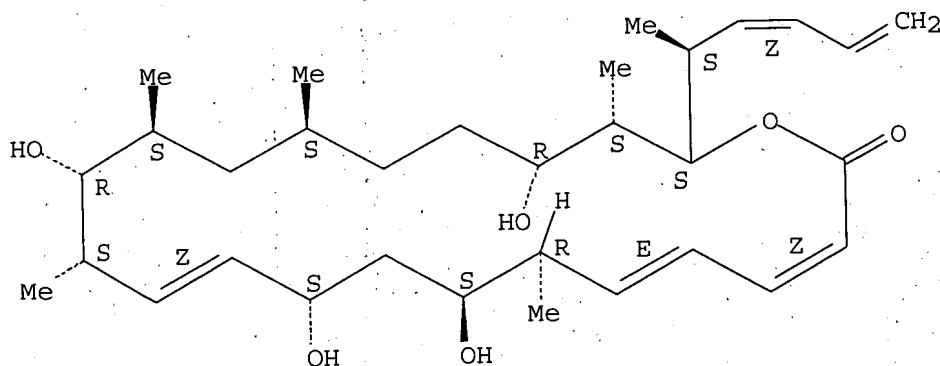
W. CA JP

PT, SE, TR
 CA 2400896 AA 20010830 CA 2001-2400896 20010226
 US 2001056118 A1 20011227 US 2001-793323 20010226
 US 6576658 B2 20030610
 EP 1259245 A2 20021127 EP 2001-911183 20010226
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI, CY, TR
 JP 2003523383 T2 20030805 JP 2001-561306 20010226
 US 2003153615 A1 20030814 US 2003-360200 20030206
 US 6677370 B2 20040113
 PRIORITY APPLN. INFO.: US 2000-184617P P 20000224
 US 2001-793323 A3 20010226
 WO 2001-US6198 W 20010226

AB Dictyostatin-1 has been found to stabilize microtubules and prohibit their depolymn. to free tubulin. Because of these activities, the dictyostatin compds. can be used in the treatment of a number of diseases in which aberrant cellular proliferation occurs such as drug-sensitive and drug-resistant cancers, autoimmune disorders, and inflammatory diseases. Dictyostatin-1 was isolated from Corallistidae sponges and the antitumor activity studied.

IT **156312-07-1P**, dictyostatin 1
 RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
 (dictyostatin compds. for stabilization of microtubules)
 RN 156312-07-1 CAPLUS
 CN Oxacyclodocosa-3,5,11-trien-2-one, 8,10,14,20-tetrahydroxy-7,13,15,17,21-pentamethyl-22-[(1S,2Z)-1-methyl-2,4-pentadienyl]-, (3Z,5E,7R,8S,10S,11Z,13S,14R,15S,17S,20R,21S,22S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
 Double bond geometry as described by E or Z.



L3 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 1995:733500 CAPLUS
 DOCUMENT NUMBER: 123:139562
 TITLE: Isolation and structure of dictyostatin 1
 INVENTOR(S): Pettit, George R.; Cichacz, Zbigniew A.
 PATENT ASSIGNEE(S): Arizona State University, USA
 SOURCE: U.S., 8 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

US 5430053
CA 2146880
EP 680958

A 19950704
AA 19951020
A1 19951108

US 1994-229658
CA 1995-2146880
EP 1995-302510

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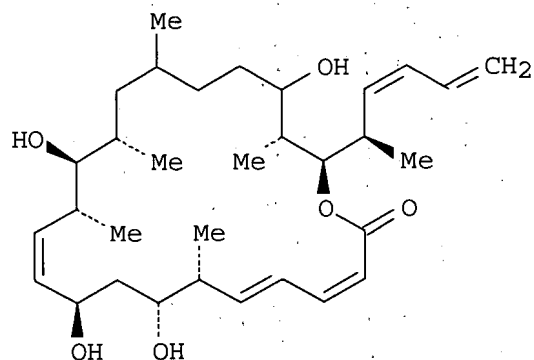
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.:

US 1994-229658

A 19940419

GI



I

AB A new-type of macrocyclic lactone denominated dictyostatin 1 (I), bearing a membered ring system, is isolated from a Republic of Maldives marine sponge in the genus *Spongia* sp. and found to strongly inhibit the growth of an important selection of U.S. National Cancer Institute human cancer cell system and the murine P388 lymphocytic leukemia (PS ED50 3.8 + 10-4 mg/mL).

IT 156312-07-1; Dictyostatin 1

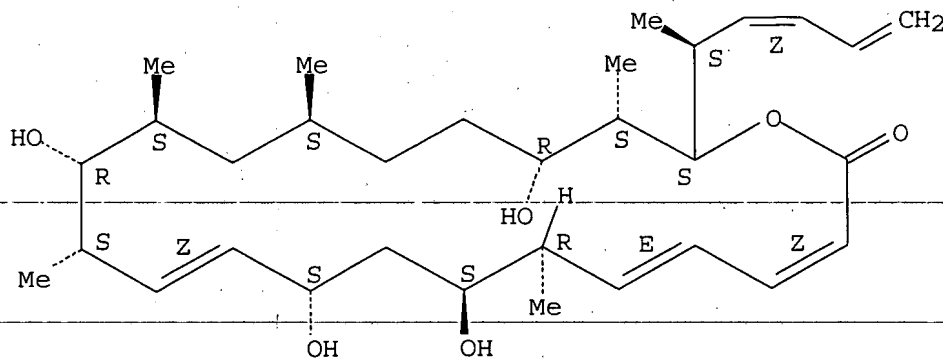
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses) (dictyostatin isolation and structural characterization and cytotoxic activity from marine sponge)

RN 156312-07-1 CAPLUS

CN Oxacyclodocosa-3,5,11-trien-2-one, 8,10,14,20-tetrahydroxy-7,13,15,17,21-pentamethyl-22-[(1S,2Z)-1-methyl-2,4-pentadienyl]-, (3Z,5E,7R,8S,10S,11Z,13S,14R,15S,17S,20R,21S,22S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Double bond geometry as described by E or Z.



inhibitor dictyostatin 1

AUTHOR(S): Pettit, George R.; Cichacz, Zbigniew A.; Gao, Feng;
Boyd, Michael R.; Schmidt, Jean M.

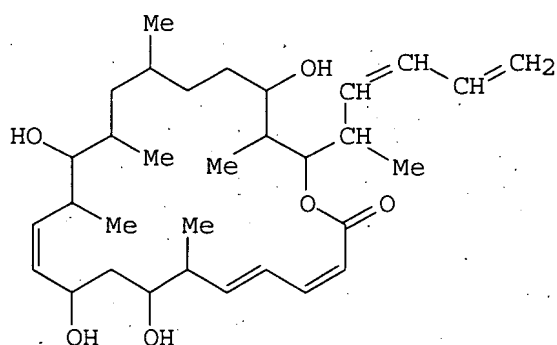
CORPORATE SOURCE: Cancer Res. Inst., Arizona State Univ., Tempe, AZ,
85287-1604, USA

SOURCE: Journal of the Chemical Society, Chemical
Communications (1994), (9), 1111-12
CODEN: JCCCAT; ISSN: 0022-4936

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

- AB Dictyostatin 1 (I), a new type of macrocyclic lactone bearing a 22-membered ring system, has been isolated (3.4 + 10⁻⁷% yield) from a Republic of Maldives marine sponge in the genus *Spongia* and found to strongly inhibit growth of the murine P388 lymphocytic leukemia.
- IT 156312-07-1; Dictyostatin 1
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
BIOL (Biological study); OCCU (Occurrence)
(of marine sponge, isolation and structure of)
- RN 156312-07-1 CAPLUS
- CN Oxacyclodocosa-3,5,11-trien-2-one, 8,10,14,20-tetrahydroxy-7,13,15,17,21-pentamethyl-22-[(1S,2Z)-1-methyl-2,4-pentadienyl]-, (3Z,5E,7R,8S,10S,11Z,13S,14R,15S,17S,20R,21S,22S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.

